ABSTRACT

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Title of Thesis: Iron-chelating properties of selected novel chelators from 4-acyl-5-pyrazolone group

Both iron deficiency and iron overload play important roles in the pathophysiology of certain diseases. A suitable therapy in the case of iron overload represents the administration of iron chelators, especially in the treatment of hematological diseases, where the chronic iron overload occurs (a long-term usage of blood transfusions). The application of iron chelators for other diseases (acute myocardial infarction, cancer, etc.) appears as a promising tool as well. The current chelators suffer from a low level of compliance, efficiency, their poor activity in acidic environment or they reduce ferric ions to ferrous ions and that leads to oxidative stress.

The subject of this thesis is to verify the iron-chelating properties of selected novel chelators from 4-acyl-5-pyrazolone group by use of UV-VIS spectrophotometric methods. Four compounds have been chosen: benzyl-, phenyl- and thienylderivatives of the basic structure and the derivative marked as H2Q4, which is a double molecule of the basic structure of 4-acyl-5-pyrazolone.

All of the tested substances had some potential to chelate ferrous ions and were also devoid of the ability to reduce ferric ions. This was verified by the ferrozin method. The most effective chelator was H2Q4 that chelated iron ions at all the range of tested pH levels (4.5-7.5), and ferric ions at pH 4.5 with the probable ratio of 2:1. Other chelators were unambiguously less effective in the chelation of ferrous ions. But their ability to bind ferric ions at pH 4.5 approached H2Q4. In respect of the impossibility to analyze ferric ions chelation at higher pHs by the ferrozin method, additional experiments were done, which verified the ability of H2Q4 to chelate ferric ions at high pHs too.

The results show that H2Q4 has the potential to be a suitable iron chelator (good affinity for the ferrous and ferric ions, the ability to chelate iron at low levels of pH, the

absence of ferric ions reduction) and thus appears promising for further preclinical trials.

KEYWORDS:

Iron, iron chelators, 4-acyl-5-pyrazolones